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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

EPPS FORD, JANET L

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/789,526	Applicant(s) DOBIE ET AL.	
	Examiner Janet L. Epps-Ford	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-7,9,13,20-23,46,47,50,52-62 and 66-73 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4-7,9,13,20-23,46,47,50,52-62 and 66-73 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10-24-08</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1, 4-7, 9, 13, 20-23, 46-47, 50, 52-62, and 66-73 are pending for examination.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

Claim Rejections - 35 USC § 103

3. Claims 1, 4-7, 9, 13, 20-23, 46-47, 50, 52-62, and 66-73 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Shoshan et al. (WO0210449) in view of Bennett et al. US Patent No. 6172216, and Wengel et al., for the reasons of record.
4. Applicant's arguments filed 10-24-08 have been fully considered but they are not persuasive. Applicants traversed the instant rejection on the grounds that the disclosures regarding antisense in Shoshan et al. are generic in nature, and do not suggest designing antisense to any particular oligonucleotide of the invention, or specifically to SEQ ID NO: 28624. According to Applicants, the disclosure of Shoshan et al. does not mention SEQ ID NO: 28624, or any other sequence in the specification of this reference. However, Applicants admit that Shoshan et al. discloses a genus of antisense based on the "oligonucleotides of the present invention."
5. According to Applicants, the Examiner failed to provide any reason why one of ordinary skill in the art would find it obvious to select the antisense oligonucleotide of the pending claims out of the at least 1.3 million member genus disclosed in Shoshan et al.

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6. Contrary to Applicant's assertions, although Shoshan et al. generically states that using known techniques, "an antisense RNA based upon the oligonucleotides of the present invention can be employed to inhibit or prevent translation of an mRNA at the cellular level," there is no rationale why this statement would not be readily applicable to an explicitly described species of the oligonucleotides of Shoshan et al., namely SEQ ID NO: 28624. The oligonucleotides of Shoshan et al. are individually described by sequence in the sequence listing attached to the reference.

7. Moreover, Applicant's own specification generically make references to oligonucleotides of their invention, see, page 14, beginning at line 20 of the specification as filed, wherein Applicants refer to the "compounds, preferably oligonucleotides and similar species for use in modulating the function or effect of nucleic acids molecules encoding growth hormone receptor..." However, Applicants have no difficulty in associating these broad references with every species of oligonucleotide disclosed in the specification as filed. In a similar manner, although a generic reference is made regarding the ability of the oligonucleotides of Shoshan et al. to be used to design antisense or siRNA, the ordinary skilled artisan reading the Shoshan et al. reference would also have a reasonable expectation, absent evidence of unexpected results, that this generic reference would also apply to the specifically disclosed species of oligonucleotide disclosed in this reference.

8. The Shoshan et al. reference was identified by means of searching SEQ ID NO: 19 of the instant invention, wherein SEQ ID NO: 28624 was identified as fully encompassing SEQ ID NO: 19. The only difference between the prior art sequence and

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the compound of claim 1, was a difference in 15 base pairs. It was not the generic disclosure of the oligonucleotides of Shoshan et al. that identified this reference as potential prior art, it was the specifically disclosed sequence of SEQ ID NO: 28624. Furthermore, the disclosure of Shoshan et al. explicitly provides motivation to use all of the specifically disclosed sequences as potential templates for designing antisense and/or siRNA compounds. Applicant's arguments are not persuasive, since Applicants have not provided any evidence why the ordinary skilled artisan would not have expected that the sequence of SEQ ID NO: 28624 would not have served as an equivalent target for designing antisense/siRNA among the broad genus of oligonucleotides explicitly described as all potentially serving this purpose.

9. Additionally, it is noted that the Shoshan et al. reference was applied as a 103 reference in view of Bennett et al. and Wengel et al. However, Applicants continue to argue the deficiencies of Shoshan et al. individually as not teaching the claimed invention.

10. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

11. Furthermore, in contrast to Applicant's assertions, since the target sequence of Shoshan et al. was disclosed in the prior art, wherein the target sequence is only 65 base pairs in length, it would have been within the level of the ordinary skilled artisan at

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the time of the instant invention, following the teachings of Bennett et al. and Wengel et al. to design antisense compounds of 12 to 50 base pairs in length targeting the 65 base pair oligonucleotide sequence of Shoshan et al. One of ordinary skill in the art would have been motivated to design the compounds of the instant invention, since the target sequence of Shoshan et al. is explicitly disclosed, and the number of potential members of the genus of antisense compounds of 12 to 50 nucleotides comprising an 8-nucleobase contiguous stretch of the 65 nucleotides of SEQ ID NO: 28624 can be readily envisioned. Moreover, due to the small number of nucleotides set forth in SEQ ID NO: 28624, and the fact that Bennett et al. teach that antisense oligonucleotides are preferably 20 base pairs in length, the sequence of SEQ ID NO: 19 of the instant invention could be immediately envisioned due to the limited number of possible 20 base pair non-overlapping antisense oligonucleotides that could be designed based upon a sequence of only 65 base pairs.

12. Additionally, it would have been obvious to design antisense oligonucleotides comprising the various modifications recited in the instant claims, particularly wherein the claimed oligonucleotide comprising a chimeric structure including a stretch of deoxynucleotides flanked by 2'-O-methoxyethyl modifications, phosphorothioate internucleoside linkages, and 5-methylcytosines, since Bennett et al. clearly teach that oligonucleotides comprising this structure are disclosed as having increased nuclease stability and increased cellular uptake. Moreover, it would have been obvious to design compounds comprising locked nucleosides comprising a bridge between the 2'-O and the 4' carbon atom. Oligonucleotides comprising this modification are

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described as forming duplexes with higher specificity with its target, and having increased thermostability with its target in comparison to un-modified oligonucleotides.

Regarding the rationale for combining prior art elements according to known methods to yield predictable results, all of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Conclusion

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/
Primary Examiner, Art Unit 1633

/J. L. E./
Primary Examiner, Art Unit 1633